

**BAKER BOTTS LLP.**

Atty. Docket No. A33432 (070050.1354)

**REMARKS**

This paper is in response to the non-final Office Action dated February 13, 2004. Applicants have included with this Reply a Declaration of Dr. Shanta M. Modak pursuant to 37 C.F.R. § 1.132 (hereinafter "Rule 132 Declaration"). Applicants respectfully assert that this Reply and Rule 132 Declaration are fully responsive to each of the objections raised in the outstanding Office Action.

Claims 1-13 and 17-24 were pending in the application. Claims 1-8, 10, 12, 13 and 17-22 have been amended. Claims 9, 11, 14, 15 and 16 have been canceled. New claims 23-24 have been added and are fully supported by the originally filed claims and the specification. See e.g., instant specification at pages 5-6. As such, claims 1-8, 10, 12, 13 and 17-24 are pending.

Each of the pending claims stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over United States Patent No. 6,261,271 to Solomon et al. (hereinafter "Solomon") alone and/or over Solomon in view of the Merck Index. The Office Action also reiterates the rejection of claims 1-2, 8-9, 17 and 21-22 under the judicially created doctrine of obvious type double patenting as being unpatentable over claims 1-4 of co-pending Application No. 09/746,658. Applicants respectfully traverse the double patenting rejection until such time as a claim in the instant application is allowed.

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**THE CLAIMED INVENTION IS NOT OBVIOUS OVER SOLOMON**

The Examiner has rejected claims 1-13 and 17-22 under 35 U.S.C. §103(a) as allegedly being unpatentable over Solomon. Solomon discloses an anti-infective medical article that "has chlorhexidine bulk distributed throughout a polyurethane base layer and may have a coating on the base layer." See Solomon Abstract. Solomon further discloses that the optional coating may be achieved by steeping the article in a solvent solution of chlorhexidine. See Solomon col. 5 at lines 49-50. Solomon does not disclose or suggest treating a catheter with a solution of chlorhexidine free base and water-soluble chlorhexidine salt, which provides sustained anti-microbial effectiveness through an increased uptake of chlorhexidine into the catheter, as required by the presently claimed invention. Nor does Solomon disclose or suggest catheters that are prepared by such treatment. In light of this information and the Rule 132 Declaration attached hereto, Applicants assert that the claimed invention is not obvious in view of Solomon.

The Office Action also states that "[a]bsent unexpected results, it is the position of the Examiner [that] it would have been obvious to one of ordinary skill in the art at the time the invention was made to have determined a suitable weight % of chlorhexidine free base and water-soluble chlorhexidine salt." (Office Action at page 4). Thus, this rejection appears to focus on a purported lack of a showing of unexpected results. However, unexpected results are a secondary consideration and only one factor to be considered in the underlying factual analysis in an obviousness inquiry. Graham v. John

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Deere Co., 383 U.S. 1, 17 (1966). Evidence indicating that unexpected results exist is typically used by an applicant to rebut a *prima facie* showing of obviousness. In re Roufett, 149 F.3d 1350, 1355 (Fed. Cir. 1998). In order to show a *prima facie* case of obviousness, the Examiner must present specific objective evidence that the prior art would have taught or suggested to one of ordinary skill in the art how to make the claimed invention. In re Deuel, 51 F.3d 1552, 1557 (Fed. Cir. 1995). Applicants respectfully assert that the rejections fail to state at minimum the requisite motivation to combine the cited references, and thus do not constitute a *prima facie* case of obviousness. Therefore, absent a *prima facie* showing of obviousness, Applicants have no burden to demonstrate that the claimed invention stems from an unexpected finding. Nevertheless, Applicants fully respond herein by this Reply and the attached Rule 132 Declaration which evidences that the catheters of the invention demonstrated unexpectedly prolonged antimicrobial activity.

The claimed invention exhibits unexpected results. As set forth in the attached Rule 132 Declaration, a catheter that has only been surface-treated as claimed by the instant invention would not have been expected by one of ordinary skill in the art to exhibit prolonged antimicrobial efficacy. Notably, Solomon's teachings admit as much. Solomon specifically taught that by merely coating the surface of the medical device with chlorhexidine, one would observe a rapid release of the chlorhexidine from the surface. See Solomon col. 3 at lines 20-21. Dr. Modak's conclusions with respect to the level of skill in the art, as stated in the attached Rule 132 Declaration, are fully consistent with

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Solomon's teachings which demonstrate that a person of ordinary would not have expected microbial effectiveness of a chlorhexidine-coated catheter in the clinic. Thus, both the attached Rule 132 Declaration and Solomon's own teachings evidence that one of ordinary skill in the art at the time of the present invention could have only expected failure in preventing microbial infection when using such catheters.

**THE CLAIMED INVENTION IS NOT OBVIOUS OVER SOLOMON IN VIEW OF THE MERCK INDEX**

Claims 1-13 and 17-22 also stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Solomon in further view of the Merck Index. The instant Office Action appears not to address Applicants' prior arguments of record which objected to the obviousness rejection on the basis of Solomon in view of the Merck Index. Nevertheless, Applicants take this opportunity to restate the arguments made in the response to the prior Office Action, which was submitted to the U.S. Patent and Trademark Office on December 23, 2003.

The Examiner again posits that:

"Absent unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Solomon by adding tetrahydrofuran taught by the Merck Index with the solvents taught by Solomon, because tetrahydrofuran is a known solvent used for polymers and is miscible with water and alcohols as taught by the Merck Index."

This statement does not constitute a *prima facie* case of obviousness. Nowhere does either Solomon or the Merck Index provide the required motivation to one of ordinary skill in the art to combine the two references to make the claimed invention. As noted in the Rule 132

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Declaration, there are numerous solvents that exhibit characteristics similar to that of tetrahydrofuran. Importantly, many of these solvents are likely to be ineffective, inappropriate, or toxic (even dangerous) for the intended use in human patients. To the extent that any criteria for a suitable solvent has been proposed in the Office Action (for example, "solvent for high polymers" or "miscible with water, alcohols, ketones, esters, ethers and hydrogen"), the number of solvents falling within such broad parameters would provide no guidance and leave the skilled artisan to empirically test each and every compound in preclinical and/or clinical trials to discriminate suitable from inoperative solvents. This lack of guidance cannot be a basis for providing any motivation to choose tetrahydrofuran, or to combine tetrahydrofuran with a "high polymer" for administration of the proposed combination to humans.

Thus, the presence of tetrahydrofuran in the Merck Index coupled with the existence of Solomon does not provide a suggestion to combine those references to arrive at the claimed invention. Instead, the Office Action impermissibly attempts to recreate the claimed invention by piecing the claimed elements together only in hindsight.

Furthermore, even if a person of ordinary skill in the art may have been motivated to try tetrahydrofuran as a solvent in the present invention, that is not the proper standard for obviousness; instead the standard is whether a person of ordinary skill in the art would have a reasonable expectation of success using the claimed solvent. See e.g., In re Antonie, 559 F.2d 618, 620 (C.C.P.A. 1977) (obvious to try is not the standard of 35

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U.S.C. § 103(b)); In re Merck & Co., Inc., 800 F.2d 1091, 1097 (Fed. Cir. 1986) ("[T]he board's decision was premised on an impermissible obvious to try standard."). The Office Action does not articulate the specific motivation to combine the cited references, and does not explain why a person of ordinary skill in the art would have reasonably expected success in making and/or using the claimed invention. As indicated in the attached Rule 132 Declaration, Applicants re-assert that no such reasonable expectation of success existed at the time of the present invention.

**CONCLUSION**

Applicants believe that in light of the foregoing amendments and remarks, the claims are in condition for allowance, and accordingly, respectfully request withdrawal of the outstanding rejections. An allowance is earnestly sought.

Respectfully submitted,



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Attachments

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